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Search History

DATE: Tuesday, September 28, 2004 [Printable Copy](#) [Create Case](#)

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result set

DB=PGPB; PLUR=YES; OP=OR

<u>L10</u>	L8 and GDF	13	<u>L10</u>
<u>L9</u>	L8 and permanent cartilage	8506	<u>L9</u>
<u>L8</u>	L7 and BMP	100	<u>L8</u>
<u>L7</u>	L6 and bioresorbable	310	<u>L7</u>
<u>L6</u>	L5 and biocompatible	7867	<u>L6</u>
<u>L5</u>	L4 and osteogenic protein	71414	<u>L5</u>
<u>L4</u>	nonarticular cartilage repair	39570	<u>L4</u>
<u>L3</u>	cartilage repair	39569	<u>L3</u>
<u>L2</u>	2003033022	0	<u>L2</u>

DB=USPT; PLUR=YES; OP=OR

<u>L1</u>	2003033022	0	<u>L1</u>
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END OF SEARCH HISTORY

Abstract Paragraph:

Polymer-bioceramic structures are described for use in the repair of bone defects. The composites of the present disclosure are characterized by a polymer disposed in a porous bioceramic matrix. Processes for preparing the composites of the present invention by compression molding are described, including compression molding to induce orientation of the polymer in multiple directions. The composites of the present invention are also useful as drug delivery vehicles to facilitate the repair of bone defects.

Summary of Invention Paragraph:

[0002] This invention pertains to polymer-bioceramic structures for use in the repair of bone. The structures are load bearing and may also be useful as drug delivery vehicles to facilitate the repair of bone defects. Processes for preparing the polymer-bioceramic structures by compression molding are described.

Summary of Invention Paragraph:

[0003] The repair of bone defects is often accelerated by placing prosthetic implants in the defect site. If the prostheses are capable bearing loads associated with normal activity, such prostheses may alleviate the problems caused by prolonged, non-weight-bearing immobilization following injury, as well as decrease costs associated with extended hospitalization. Both naturally-occurring and artificially-produced prosthetic implants have been used to repair such defects. Naturally-occurring materials include grafts made from bones. The bone may be harvested directly from the patient, as in autograft-based procedures, or it may be harvested from a suitable donor, surrogate, or cadaver, as in allograft-based procedures. Natural bone is an ideal source of graft material not only for its biocompatibility, but also because natural bone grafts facilitate reossification of the defect site by promoting or conducting ingrowth of the patient's own bone tissue into the defect site. However, autograft bone implant procedures may be unavailable to certain patients who would be placed at increased risk by such procedures, typically requiring two surgical operations. Moreover, many of these patients, especially osteoporotic patients, are already compromised, and may not have a sufficient source of good quality bone that may be used for graft material.

Summary of Invention Paragraph:

[0004] Research has been directed toward the development of synthetic sources of material for use in bone defect repair. The design of a synthetic material that is chemically and morphologically similar to natural bone and exhibits similar mechanical properties is thought to provide the best source of graft material to repair most defects. The empirical composition of the mineral component of natural bone is:

Summary of Invention Paragraph:

[0011] In addition to bioceramic materials, organic polymers have been used as bone defect repair materials, including poly(methyl methacrylate) (PMMA), poly(lactic acid) (PLA), and poly(glycolic acid) PGA. PMMA, also commonly used as a bone cement, is not subject to degradation by most biological processes in the patient. However, PMMA-based compositions have been made partially resorbable by including cross-linked poly(propylene glycol fumarate) (PPF) and a particulate bioceramic, as described by Gerhart et al., in U.S. Pat. Nos. 5,085,861 and 4,843,112. However, these cements are primarily designed to be used in conjunction with the implantation of other non-resorbable prosthetic devices. Bone ingrowth into the cement helps to achieve better mechanical lock of those prostheses, though such ingrowth is typically limited to the exposed surface of the cement. In other variations, composite bone cements incorporating a bioresorbable particulate compound with a non-biodegradable polymeric resin are described by Draenert, in U.S. Pat. No. 4,373,217.

Summary of Invention Paragraph:

[0012] The present invention encompasses bioresorbable and implantable structures for use in the repair of bone defects. The structures comprise a porous bioceramic matrix and a polymer disposed therein.

The polymer is disposed in the void volume created by the porous nature of the matrix, and is illustratively oriented in the pores. The bioceramic is illustratively an inorganic salt that includes the ions of calcium and phosphate, and in other aspects the bioceramic includes sulfate and carbonate. The polymer is illustratively a synthetic polymer, or a naturally occurring polymer, including polypeptides. Certain structures described herein are capable of being substantially or even completely reabsorbed by the patient via endogenous biochemical, biological, and metabolic processes, leading to a prosthesis that does not require subsequent removal following treatment of the bone defect.

Summary of Invention Paragraph:

[0015] The structures are also useful for delivering drugs to defect sites, including agents that facilitate or enhance the growth of bone, such as osteogenic agents, proteins involved in bone growth, and populations of cells. Substances capable of enhancing the effectiveness of the drugs may also be included. The structures may be used in a variety of defects, such as bone voids, fractures, maxillofacial defects, periodontal defects, and defects related to or arising from the removal of a bone or bone tumors.

Detail Description Paragraph:

[0016] The present disclosure encompasses bioresorbable and implantable structures for use in the repair of bone defects. The structures described herein comprise a porous bioceramic matrix and a polymer. The polymer is disposed in the porous bioceramic matrix.

Detail Description Paragraph:

[0017] Bioceramics useful in the invention are substantially non-toxic, biodegradable, bioerodable, and bioresorbable. The terms "biodegradable" and "bioerodable" as used herein similarly refer to a material property where biological, biochemical, metabolic processes, and the like may effect the erosion or degradation of the material over time. Such degradation or erosion is due, at least in part, to contact with substances found in the surrounding tissues, body fluids, and cells, or via cellular action, enzymatic action, hydrolytic processes, and other similar mechanisms in the body. The term "bioresorbable" as used herein refers to materials that are used by, resorbed into, or are otherwise eliminated from the body of the patient via existing biochemical pathways and biological processes. For example, in embodiments where the bioceramic comprises calcium phosphate, bioresorbed calcium phosphate may be redeposited as bone mineral, be otherwise reutilized within the body, or be excreted. It is understood that some materials become bioresorbable following biodegradation or bioerosion of their original state, as described above.

Detail Description Paragraph:

[0018] The term "biocompatible" as used herein refers to material that does not elicit a substantial detrimental response in the host, including but not limited to an immune reaction, such as an inflammatory response, tissue necrosis, and the like that will have a negative effect on the patient.

Detail Description Paragraph:

[0019] The salts used to prepare the bioceramics and the bioceramic matrices, fabricated therefrom are commercially available or are readily prepared via known procedures. Bioceramics include calcium salts of carbonate, sulfate, phosphate, and the like. Exemplary bioresorbable calcium salts effective in the composition of this invention include calcium carbonate, calcium sulfate, calcium sulfate hemihydrate, also known as plaster of Paris, and certain porous or precipitated forms of calcium phosphate, and the like. The porous bioceramic matrix may also be fabricated from any number of natural bone sources, such as autograft or allograft material, or synthetic materials that are compositionally related to natural bone.

Detail Description Paragraph:

[0028] Polymers useful in the invention are preferably non-toxic, biocompatible, biodegradable, and bioresorbable, i.e., their degradation products are used by or are otherwise eliminated from the body of the treated subject via existing biochemical pathways and biological processes. The monomers used to prepare the polymers, and in some cases the polymers themselves, that are employed in the structures described herein are available commercially or are readily prepared through known procedures. Such polymers may be synthetic or naturally occurring, or may be polymer blends or copolymers.

Detail Description Paragraph:

[0029] Thermoplastic polymers useful herein include pharmaceutically-compatible polymers that are biodegradable, bioresorbable, and soften when exposed to heat but return to the original state when cooled. Examples include polylactides, polyglycolides, polycaprolactones, polyanhydrides, polyamides, polyurethanes, polyesteramides, polyorthoesters, polydioxanones, polyacetals, polyketals, polycarbonates, polyorthoesters, polyphosphazenes, polyhydroxybutyrates, polyhydroxyvalerates, polyalkylene oxalates, polyalkylene succinates, poly(malic acid), poly(amino acids), poly(methyl vinyl ether), poly(maleic anhydride), and copolymers, terpolymers, or combinations or mixtures therein.

Detail Description Paragraph:

[0030] Certain polyesters, polyanhydrides, polyorthoesters, and the like may be used in the structures described herein. See U.S. Pat. No. 3,997,512 to Casey et al. (biodegradable polyester resin prepared by esterifying diglycolic acid with an unhindered glycol, providing self-supporting film forming properties for drug delivery); U.S. Pat. No. 4,181,983 to Kulkarni (biodegradable, assimilable, hydrophilic bandage for a dry socket in dental therapy); U.S. Pat. No. 4,481,353 to Nyilas et al. (Bioresorbable polyesters composed of the Krebs Cycle components, such as succinic acid, fumaric acid, oxaloacetic acid, L-malic acid, and D-malic acid, and a diol, such as glycolic acid, L-lactic acid, and D-lactic acid); and U.S. Pat. No. 4,452,973 to Casey et al. (Poly(glycolic acid)/poly(oxyalkylene) ABA triblock copolymers), the disclosures of which are incorporated herein by reference.

Detail Description Paragraph:

[0035] In addition, it is understood that polymers, copolymers, and polymer blends used in the structures described herein may be selected for particular drug release characteristics, mechanical reinforcement capabilities, or mechanical properties such as elasticity, or combinations thereof depending on the desired configuration of the structure. Still other bioresorbable organic polymers are described in U.S. Pat. Nos. 5,385,887, 4,578,384, 4,563,489, 4,637,931, 4,578,384, and 5,084,051, the disclosures of which are incorporated herein by reference.

Detail Description Paragraph:

[0036] Structures described herein are desirably chemically biocompatible; capable of supporting a load; accept or facilitate bone ingrowth promoting good mechanical interlock; and capable of complete or near complete resorption by the patient and contemporaneous replacement by natural bone in the patient.

Detail Description Paragraph:

[0037] Biocompatible calcium phosphate ceramics are selected particularly in bone repair embodiments for their properties to promote interfacial osteoconduction. Bone ingrowth is facilitated by an embodiment where the bioceramic matrix is a three-dimensional scaffold possessing pores, interstices, pockets, channels, passages, tunnels, and the like. In some aspects, these interstices, pockets, channels, passages, tunnels, and the like comprise a major portion, or a substantial portion of the volume possessed by the porous bioceramic matrix. In other aspects, these interstices, pockets, channels, passages, tunnels, and the like comprise less than 50% of the volume possessed by the porous bioceramic matrix.

Detail Description Paragraph:

[0042] While it is appreciated that the above-described composition may also elicit osteogenic behavior on its own, another embodiment is a structure that may be used as a drug delivery system. Either the polymer, the bioceramic, or both may include a biologically-active agent, either singly or in combination, such that the composite structure or implant will provide a delivery system for the agent. The agent may be delivered to adjacent tissues or tissues proximal to the implant site. Biologically-active agents which may be used alone or in combination in the implant precursor and implant include, for example, a medicament, drug, or other suitable biologically-, physiologically-, or pharmaceutically-active substance which is capable of providing local or systemic biological, physiological, or therapeutic effect in the body of the patient. The biologically-active agent is capable of being released from the solid implant matrix into adjacent or surrounding tissue fluids during biodegradation, bioerosion, or bioresorption as described above.

Detail Description Paragraph:

[0043] In one aspect, the biologically-active agent is an osteogenic agent. Each component substance, the bioceramic matrix material or the polymer, may be osteogenic; or the combination of the bioceramic matrix material with the polymer forming the structure described above may be osteogenic.

Detail Description Paragraph:

[0044] The term "osteogenic agent" as used herein refers to agents that promote, induce, stimulate, generate, or otherwise effect the production of bone or the repair of bone. The presence of an osteogenic agent in the defect site may elicit an effect on the repair of the defect in terms of shortening the time required to repair the bone, by improving the overall quality of the repair, where such a repair is improved over situations in which such osteogenic agents are omitted, or may achieve contemporaneously both shortened repair times and improved bone quality. It is appreciated that osteogenic agents may effect bone production or repair by exploiting endogenous systems, such as by the inhibition of bone resorption.

Detail Description Paragraph:

[0045] Osteogenic agents may promote bone growth by acting as bone anabolic agents. Compositions of the present invention may also effect repair of the bone defect by stabilizing the defect to promote healing. The ramifications of using such osteogenic agents include increased healing rates, effecting a more rapid new bone ingrowth, improved repair quality, or improved overall quality of the resulting bone.

Detail Description Paragraph:

[0046] In one embodiment the osteogenic agent is a "small molecule" such as a synthetic molecule, drug, or pharmaceutical involved in, or important to, bone biology, including statins, such as lovastatin, simvastatin, atorvastatin, and the like, fluprostenol, vitamin D, estrogen, a selective estrogen receptor modifier, or a prostaglandin, such as PGE-2. Combinations of such small molecules in providing the osteogenic agent are contemplated herein.

Detail Description Paragraph:

[0047] In another embodiment the osteogenic agent is a "large molecule" such as an endogenous-derived protein or other protein, an enzyme, a peptide, receptor ligand, a peptide hormone, lipid, or carbohydrate involved in, or important to, bone physiology, including the bone morphogenic or bone morphogenetic proteins (BMPs), such as BMP-2, BMP-7, and BMP-9, chrysalin, osteogenic growth peptide (OGP), bone cell stimulating factor (BCSF), KRX-167, NAP-52, gastric decapeptide, parathyroid hormone (PTH), a fragment of parathyroid hormone, osteopontin, osteocalcin, a fibroblast growth factor (FGF), such as basic fibroblast growth factor (bFGF) and FGF-1, osteoprotegerin ligand (OPGL), platelet-derived growth factor (PDGF), an insulin-like growth factor (IGF), such as IGF-1 and IGF-2, vascular

endothelial growth factor (VEGF), transforming growth factor (TGF), such as TGF-alpha and TGF-beta, epidermal growth factor (EGF), growth and differentiation factor (GDF), such as GDF-5, GDF-6, and GDF-7, thyroid-derived chondrocyte stimulation factor (TDCSF), vitronectin, laminin, amelogenin, amelin, fragments of enamel, or dentin extracts, bone sialoprotein, and analogs and derivatives thereof. Combinations of such large molecules in providing the osteogenic agent are contemplated herein.

Detail Description Paragraph:

[0048] In another embodiment the osteogenic agent is a cell or population of cells involved in, or important to, bone biology, such as pluripotent stem cells, autologous, allogenic, or xenogeneic progenitor cells, chondrocytes, adipose-derived stem cells, bone marrow cells, mesenchymal stem cells, homogenized or comminuted tissue transplants, genetically transformed cells, and the like. Bone powders, including demineralized bone powders and bone matrix, may also be used. Combinations of such cell populations in providing the osteogenic agent are also contemplated herein.

Detail Description Paragraph:

[0049] Depending upon its nature, the osteogenic agent may be present in the structure within the range from about 0.1% to about 30% by weight, preferably in the range from about 1% to 9% by weight.

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Search Results - Record(s) 1 through 10 of 13 returned.

☐ 1. Document ID: US 20040093164 A1

L10: Entry 1 of 13

File: PGPB

May 13, 2004

PGPUB-DOCUMENT-NUMBER: 20040093164

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040093164 A1

TITLE: Computer system and methods for producing morphogen analogs of human TDF-1

PUBLICATION-DATE: May 13, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Carlson, William D.	Weston	MA	US	
Keck, Peter C.	Millbury	MA	US	

US-CL-CURRENT: 702/19

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KIMC	Draw De
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☐ 2. Document ID: US 20040002770 A1

L10: Entry 2 of 13

File: PGPB

Jan 1, 2004

PGPUB-DOCUMENT-NUMBER: 20040002770

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040002770 A1

TITLE: Polymer-bioceramic composite for orthopaedic applications and method of manufacture thereof

PUBLICATION-DATE: January 1, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
King, Richard S.	Warsaw	IN	US	
Smith, Todd S.	Fort Wayne	IN	US	

US-CL-CURRENT: 623/23.51; 264/273, 424/425

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KIMC	Draw De
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☐ 3. Document ID: US 20030185792 A1

L10: Entry 3 of 13

File: PGPB

Oct 2, 2003

PGPUB-DOCUMENT-NUMBER: 20030185792

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030185792 A1

TITLE: Morphogen analogs of bone morphogenic proteins

PUBLICATION-DATE: October 2, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Keck, Peter C.	Millbury	MA	US	
Bosukonda, Dattatreya	Shrewsbury	MA	US	

US-CL-CURRENT: 424/85.1; 435/184, 514/12, 514/44, 514/9

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw. De
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☐ 4. Document ID: US 20030176667 A1

L10: Entry 4 of 13

File: PGPB

Sep 18, 2003

PGPUB-DOCUMENT-NUMBER: 20030176667

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030176667 A1

TITLE: Single chain analogs of the TGF-beta superfamily (morphons)

PUBLICATION-DATE: September 18, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Keck, Peter C.	Millbury	MA	US	
Smart, John E.	Weston	MA	US	

US-CL-CURRENT: 530/399

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw. De
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☐ 5. Document ID: US 20030175410 A1

L10: Entry 5 of 13

File: PGPB

Sep 18, 2003

PGPUB-DOCUMENT-NUMBER: 20030175410

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030175410 A1

TITLE: Method and apparatus for preparing biomimetic scaffold

PUBLICATION-DATE: September 18, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Campbell, Phil G.	Pittsburgh	PA	US	
Weiss, Lee E.	Pittsburgh	PA	US	

US-CL-CURRENT: 427/2.24; 118/664, 435/396, 623/23.72

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMC	Draw De
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☐ 6. Document ID: US 20030109445 A1

L10: Entry 6 of 13

File: PGPB

Jun 12, 2003

PGPUB-DOCUMENT-NUMBER: 20030109445

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030109445 A1

TITLE: Methods and compositions for the treatment and prevention of parkinson's disease

PUBLICATION-DATE: June 12, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Rueger, David C.	Southborough	MA	US	
Sampath, Kuber T.	Holliston	MA	US	
Cohen, Charles M.	Weston	MA	US	
Oppermann, Hermann	Medway	MA	US	
Pang, Roy H.L.	Etna	NH	US	

US-CL-CURRENT: 514/12

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMC	Draw De
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☐ 7. Document ID: US 20030109038 A1

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File: PGPB

Jun 12, 2003

PGPUB-DOCUMENT-NUMBER: 20030109038

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030109038 A1

TITLE: Chondrocyte precursors derived from human embryonic stem cells

PUBLICATION-DATE: June 12, 2003

h e b b g e e e f e f f e f b e

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Thies, R. Scott	Pleasanton	CA	US	

US-CL-CURRENT: 435/366

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw. De
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☐ 8. Document ID: US 20030022830 A1

L10: Entry 8 of 13

File: PGPB

Jan 30, 2003

PGPUB-DOCUMENT-NUMBER: 20030022830

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030022830 A1

TITLE: Methods for enhancing functional recovery following central nervous system ischemia or trauma

PUBLICATION-DATE: January 30, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Charette, Marc F.	Needham	MA	US	
Finklestein, Seth P.	Needham	MA	US	

US-CL-CURRENT: 514/12

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw. De
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☐ 9. Document ID: US 20020173851 A1

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File: PGPB

Nov 21, 2002

PGPUB-DOCUMENT-NUMBER: 20020173851

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020173851 A1

TITLE: Intervertebral disc treatment devices and methods

PUBLICATION-DATE: November 21, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
McKay, William F.	Memphis	TN	US	

US-CL-CURRENT: 623/17.11

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw. De
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☐ 10. Document ID: US 20020155500 A1

L10: Entry 10 of 13

File: PGPB

Oct 24, 2002

PGPUB-DOCUMENT-NUMBER: 20020155500

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020155500 A1

TITLE: Morphogenic protein-specific cell surface receptors and uses therefor

PUBLICATION-DATE: October 24, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Dijke, Peter ten	Uppsala	MA	SE	
Heldin, Carl-Henrik	Uppsala		SE	
Miyazono, Kohei	Asaka-shi		JP	
Sampath, Kuber T.	Medway		US	

US-CL-CURRENT: 435/7.1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw De
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<u>L14</u>	l12 and nonarticular cartilage	9706	<u>L14</u>
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<u>L13</u>	L12 and l4	0	<u>L13</u>
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<u>L12</u>	5270300.pn.	1	<u>L12</u>
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<u>L11</u>	5270300.pn.	0	<u>L11</u>
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<u>L9</u>	L8 and permanent cartilage	8506	<u>L9</u>
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<u>L8</u>	L7 and BMP	100	<u>L8</u>
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<u>L7</u>	L6 and bioresorbable	310	<u>L7</u>
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<u>L6</u>	L5 and biocompatible	7867	<u>L6</u>
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<u>L5</u>	L4 and osteogenic protein	71414	<u>L5</u>
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<u>L3</u>	cartilage repair	39569	<u>L3</u>
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DB=USPT; PLUR=YES; OP=OR

L1 2003033022

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